REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following commentary.

I. Status of the Claims

Claim 1 has been amended to state that the claimed composition does not "incorporate a cloud point modifier." Exemplary support for this claim amendment can be found in the original specification, for example, at pages 6-7. Claims 32-35, 37 and 39 have been amended to rephrase the claimed subject matter.

Applicants acknowledge the finality of this Office Action. Nevertheless, the amendments to the claims are necessitated by the Examiner's commentary, are made to reword the claimed subject matter, and do not require any additional search. Thus, because the amendments either place the application in condition for allowance or at least in better condition for appeal, and do not introduce any new matter, Applicants respectfully request entry of this amendment. Upon entry, claims 1-45 are under examination and claims 46-123 are withdrawn.

II. Rejection of Claims under 35 U.S.C. § 112, first paragraph

Claims 35-40, 44 and 45 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of written description and enablement. Applicants respectfully traverse the rejection.

The Examiner still questions "how the composition can result in the claimed release profile, C_{max}, T_{max} and bioequivalency." As discussed in the prior response filed July 9, 2007, the increased bioavailability is achieved by decreasing the particle size of the active agent. *See,* for example, at page 1, lines 16-21; at page 4, lines 23-28; at page 5, lines 15-24; and at page 12, lines 3-10. By definition, "bioavailability" is a measurement of the rate and extent of a therapeutically active drug that reaches the systemic circulation and is available at the site of action (online Wikipedia encyclopedia). The skilled artisan would have appreciated that bioavailability is determined by a pharmacokinetic study and

represented by the plasma drug concentration *vs.* time after administration. The specification further describes that bioequivalency "is preferably established by a 90% Confidence Interval (CI) of between 0.80 and 1.25 for both C_{max} and AUC" (page 18, lines 18-25). Therefore, the specification provides written support that to achieve the claimed release profile, represented by the C_{max}, T_{max}, AUC and bioequivalency, the active ingredient must be reduced to an average particle size of less than 2000 nm and be maintained stable at this size in the presence of at least one surface stabilizer and at least one osmotically active crystal growth inhibitor, as recited in claim 1.

The specification is also enabling because it describes how to make nanoparticulate formulations (page 32 *ff*) and how the composition is stabilized in the presence of different crystal growth inhibitors (Examples 1-8).

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

III. Rejection of Claims under 35 U.S.C. § 112, second paragraph

Claims 13, 24, 32-35, 37 and 39 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. Applicants respectfully traverse the rejection.

Specifically, the Examiner alleges that claim 24 contains trademarks. In the prior response filed July 9, 2007, Applicants amended claim 24 to replace the trademarks with the corresponding generic terms. Therefore, rejection of claim 24 lacks valid basis.

The Examiner asserts that claim 13 recites the phrase of "the liquid media of the liquid dosage composition," which lacks antecedent basis. The antecedent basis for "the liquid media" and "the liquid dosage composition" is found at the last line and the first line of claim 1, respectively, from which claim 13 depends. Therefore, claim 13 is not indefinite for lack of antecedent basis for these terms.

Claims 32-34, 35, 37 and 39 are allegedly lack antecedent basis for the terms of "the viscosity," "the T_{max}," "the C_{max}," and "the AUC," respectively. Without acquiescing to the stated rational of the rejection, Applicants have amended the claims in question to reword the subject matter.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection of the claims under 35 U.S.C. § 112, second paragraph.

IV. Rejection of Claims under 35 U.S.C. § 102(b)

A. Na1

Claims 1-4, 6, 7, 10-15, 18 and 20-24 are rejected under 35 U.S.C. § 102(b) for alleged anticipation by U.S. Patent No. 5,298,262 to Na *et al.* ("Na1"). Applicants respectfully traverse the rejections.

Na1's composition requires the presence of: (a) nanoparticles of an active agent, (b) a surface modifier adsorbed on the surface of the active agent, and (c) an anionic or cationic surfactant cloud point modifier that increases the cloud point of the surface modifier. *See* the abstract. Optionally, Na1's composition comprises an isotonicity maintaining compound, which adjusts the osmotic pressure to provide a solution suitable for administration into the blood stream. The exemplary isotonicity maintaining compounds are mannitol, dextrose, sodium chloride, potassium chloride, Ringer's lactate, *etc.* *See* column 6, lines 12-32, of Na1.

In contrast to Na1's composition, the claimed composition does NOT incorporate a cloud point modifier, as prescribed by claim 1.

The Examiner, in asserting that Na1's composition "further comprises isotonicity maintaining compounds include[ing] mannitol, dextrose, and sodium chloride (crystal growth inhibitor)" (final Office Action, page 4, lines 16-17), appears to imply that the "sodium chloride"

of Na1 reads on Applicants' claimed composition comprising a crystal growth inhibitor. This interpretation of the teaching of Na1 is incorrect.

Specifically, in contrast to the Examiner's assertion, there is no teaching or suggestion in Na1 that sodium chloride, which is used as an isotonicity maintaining compound, can be used as a crystal growth inhibitor. This is significant, as the fact that a compound functions to maintain the isotonicity of a composition does not teach or suggest that the composition may also be useful in controlling crystal growth of a composition. These activities (isotonicity and crystal growth) do not have any readily apparent relationship.

Because Na1 fails to teach that removing the cloud point modifier would achieve a reduction in crystal growth of the composition at ambient temperatures, and because the rejection is based on the Examiner's misinterpretation of the art, Applicants respectfully request withdrawal of the rejection over Na1.

B. Na2

Claims 1-5, 8-15 and 17-24 are rejected under 35 U.S.C. § 102(b) for alleged anticipation by European Patent No. 0601619 to Na *et al.* ("Na2"). Applicants respectfully traverse the rejections.

Similar to Na1, Na2's composition requires the inclusion of three ingredients: (a) nanoparticles of an active agent, (b) a surface modifier adsorbed on the surface of the active agent, and (c) a non-ionic cloud point modifier that increases the cloud point of the surface modifier (abstract). The Examiner appears to allege that Na2's non-ionic cloud point modifier reads on the claimed crystal growth inhibitor (final Office Action, page 5, lines 2-3). Applicants respectfully disagree.

Na2 describes that the goal of the described invention is to prevent nanoparticles from agglomerating during autoclaving (page 2, lines 22-25). To achieve this goal, a cloud point

modifier is added to increase the cloud point of the surface modifier "above the temperature for sterilization, such as autoclaving" (page 2, lines 31-33). Moreover, the examples of Na2 demonstrate that the cloud point modifier affects the cloud point of the surface modifier at a temperature in the range between 106°C and 126°C, which is much higher than ambient temperature. Na2 has no teaching or suggestion that the cloud point modifier is able to function at ambient temperatures.

By contrast, the claimed crystal growth inhibitor can effectively inhibit crystal growth at ambient temperatures, such as at 40°C. See specification, at page 21, line 20, and the examples. Because the properties of the claimed crystal growth inhibitor are different from those of the prior-art cloud point modifier, one skilled in the art would not have equated these two substances.

Accordingly, Na2 fails to teach or suggest a composition that does not incorporate a cloud point modifier to anticipate the claimed invention. As such, Applicants respectfully request withdrawal of the rejection.

V. Rejection of Claims under 35 U.S.C. § 103(a)

Claims 1-45 are rejected under 35 U.S.C. § 103(a) for allegedly being obvious over Na1 and Na2, in view of U.S. Patent Application Publication No. 2005/0004049 to Liversidge. Applicants respectfully traverse the rejection.

As discussed above, the claimed composition does not incorporate a cloud point modifier. Na1 and Na2 teach away from the claimed invention by requiring the addition of a cloud point modifier.

The Examiner cited the secondary reference, Liversidge, for its alleged teaching of the active agent as well as C_{max}, T_{max}, bioequivalency, and viscotiy. However, Liversidge does not remedy the deficiencies of Na1 and Na2, as Liversidge does not teach the claimed composition

comprising a crystal growth inhibitor and lacking a cloud point modifier. Therefore, the prior art, alone or in combination with Liversidge, fails to teach or fairly suggest the claimed invention. Withdrawal of the rejection is warranted.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Dec 17, 2007

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